

We claim:

1. A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder, said method comprising detecting a marker that is linked to map position 4q35.2 of the human genome in a sample derived from a subject, wherein the detection is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.
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2. The method according to claim 1 wherein the marker linked to map position 4q35.2 is located between or comprises the microsatellite markers selected from the group consisting of:
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 - (i) the microsatellite marker designated D4S1164 (SEQ ID NO: 21) and the microsatellite marker D4S1192 (SEQ ID NO: 27);
 - (ii) the microsatellite marker designated D4S910 (SEQ ID NO: 22) and the microsatellite marker D4S1374 (SEQ ID NO: 28);
 - (iii) the microsatellite marker designated D4S3173 (SEQ ID NO: 23) and the microsatellite marker D4S1375 (SEQ ID NO: 29);
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 - (iv) the microsatellite marker designated D4S3236 (SEQ ID NO: 24) and the microsatellite marker designated D4S3051 (SEQ ID NO: 30); and
 - (v) the microsatellite marker designated D4S2827 (SEQ ID NO: 25) and the microsatellite marker D4S2643 (SEQ ID NO: 31).
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3. The method according to claim 1 wherein the marker linked to map position 4q35.2 is located within or comprises the FAT gene.
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4. A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder, said method comprising detecting a marker within a FAT gene or an expression product thereof that is associated with a bipolar affective disorder in a sample derived from a subject, wherein a presence of the marker is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.
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5. The method according to claim 4 wherein the FAT gene comprises a nucleotide sequence selected from the group consisting of:
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 - (i) a nucleotide sequence at least 80% identical to the nucleotide sequence set forth in SEQ ID NO: 1;

- (ii) a nucleotide sequence that encodes a mRNA at least 80% identical to the nucleotide sequence set forth in SEQ ID NO: 2 or 4; and
- (iii) a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 3 or 5.
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6. The method according to claim 4 wherein the marker is located within the 3' region of the FAT gene.
- 10 7. The method according to claim 3 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 139,260 to nucleotide position 170,001 of SEQ ID NO: 1.
- 15 8. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 146,012 to nucleotide position 170,001 of SEQ ID NO: 1.
- 20 9. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,108 to nucleotide position 170,001 of SEQ ID NO: 1.
- 25 10. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,199 to nucleotide position 170,001 of SEQ ID NO: 1.
- 30 11. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,333 to nucleotide position 170,001 of SEQ ID NO: 1.
- 35 12. The method according to claim 4 wherein the marker comprises a polymorphism in the FAT gene.

13. The method according to claim 12 wherein the polymorphism is a single nucleotide polymorphism (SNP).
- 5 14. The method according to claim 13 wherein the SNP is selected from the group consisting of a cytosine at a position corresponding to nucleotide 80,217 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 130,625 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 130,613 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 142,199 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 142,460 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 145,782 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,008 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,199 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,333 of SEQ ID NO: 1, a thymine at position 148,333 of SEQ ID NO: 1, a cytosine at a position corresponding to 148,333 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 151,403 of SEQ ID NO: 1 and a thymine at a position corresponding to nucleotide 153,127 of SEQ ID NO: 1.
15. The method according to claim 13 wherein the SNP is selected from the group consisting of a guanine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,333 of SEQ ID NO: 1 and a thymine at position 148,333 of SEQ ID NO: 1.
- 30 35 16. The method according to claim 13 wherein the subject does not have a family history of psychiatric illness and the SNP is selected from the group consisting

of a guanine at a position corresponding to 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to 148,108 of SEQ ID NO: 1 and a thymine at a position corresponding to 148,333 of SEQ ID NO: 1.

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17. The method according to claim 13 wherein the subject has a family history of psychiatric illness and the SNP is selected from the group consisting of a thymine at a position corresponding to 139,968 of SEQ ID NO: 1, an adenine at a position corresponding to 146,012 of SEQ ID NO: 1, a cytosine at a position corresponding to 148,108 of SEQ ID NO: 1 and a cytosine at a position corresponding to 148,333 of SEQ ID NO: 1.
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18. The method according to claim 4 wherein the marker comprises a nucleic acid comprising a nucleotide sequence at least about 80% identical to at least about 15 20 contiguous nucleotides in a sequence selected from the group consisting of:
 - (i) a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 4;
 - (ii) a sequence capable of encoding a polypeptide comprising an amino acid sequence at least 80% homologous to the sequence set forth in SEQ ID NO: 3 and SEQ ID NO: 5; and
 - (iii) a sequence complementary to a sequence set forth in (i) or (ii).
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19. The method according to claim 4 wherein the marker is detected by hybridising a nucleic acid probe or primer comprising the sequence of the marker to a marker linked to nucleic acid in a biological sample derived from a subject under moderate to high stringency hybridisation conditions and detecting the hybridisation using a detection means, wherein hybridisation of the probe to the sample nucleic acid indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.
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20. The method according to claim 4 wherein the marker is detected by hybridising a nucleic acid probe or primer comprising the sequence of the marker to a nucleic acid that is linked to the marker in nucleic acid in a biological sample derived from a subject under moderate to high stringency hybridisation conditions and detecting the hybridisation by a detection means, wherein
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hybridisation of the probe to the sample nucleic acid indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.

21. The method according to claim 19 or 20 wherein the detection means is a
5 nucleic acid hybridisation reaction or a nucleic acid amplification reaction.
22. The method according to claim 21 wherein the detection means is a polymerase chain reaction.
- 10 23. The method according to claim 19 or 20 wherein the nucleic acid probe or primer comprises a sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.
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24. The method according to claim 4 wherein the marker is detected by contacting a
20 biological sample derived from the subject with an antibody capable of specifically binding to said marker for a time and under conditions sufficient for an antibody-ligand complex to form and then detecting the complex wherein detection of the complex indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.
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25. The method according to claim 4 wherein the biological sample comprises a nucleated cell.
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26. The method according to claim 25 wherein the biological sample is selected from the group consisting of whole blood, serum, plasma, peripheral blood mononuclear cells (PBMC), a buffy coat fraction, saliva, urine, a buccal cell and a skin cell.
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27. The method according to claim 25 wherein the biological sample comprises a cell or cell extract or mixture thereof derived from a tissue selected from the group consisting of a brain, a spinal cord, skin, a lung, a kidney and a pancreas

28. The method according to claim 25 wherein the biological sample comprises a cell or an extract thereof or a mixture thereof isolated using a method selected from the group consisting of amniocentesis, chorionic villus sampling, fetal blood sampling and fetal skin biopsy.
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29. The method according to any one of claims 25 to 28 wherein the biological sample has been derived previously from the subject.
- 10 30. A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder in a subject, said method comprising:
- (i) amplifying nucleic acid from the subject using an amplification reaction, wherein the amplification reaction is performed using a pair of primers selected from the group consisting of:
- 15 (a) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 32 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 33;
- (b) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 34 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 35;
- 20 (c) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 36 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 37;
- (d) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 38 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 39;
- 25 (e) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 40 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 41;
- (f) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 42 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 43;
- 30 (g) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 44 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 45;
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- (h) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 46 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 47;
- 5 (i) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 48 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 49;
- (j) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 50 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 51;
- 10 (k) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 53 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 54; and
- (l) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 56 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 57;
- 15 (ii) detecting a polymorphism in the amplified nucleic acid from (i), wherein said polymorphism is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.
- 20 31. The method according to claim 30 wherein the polymorphism is detected by determining the nucleotide sequence of the amplified nucleic acid.
32. Use of a probe or primer comprising at least about 20 nucleotides that is capable of selectively hybridizing to the sequence set forth in SEQ ID NO: 1 and detecting a marker in a FAT gene that is associated with a bipolar affective disorder or a predisposition to a bipolar affective disorder in the manufacture of 25 a diagnostic reagent for determining a predisposition of a subject to a bipolar affective disorder or diagnosing a bipolar affective disorder.
- 30 33. The use according to claim 32 wherein the probe or primer comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, 35 SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID

NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.

34. A probe or primer comprising at least about 20 nucleotides that is capable of selectively hybridizing to the sequence set forth in SEQ ID NO: 1 and detecting a marker in a FAT gene that is associated with a bipolar affective disorder or a predisposition to a bipolar affective disorder.
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35. The probe or primer according to claim 34 comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36; SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.
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36. A method for determining a subject that carries a gene or allele of a gene or a polymorphism that is associated with a bipolar affective disorder comprising detecting a marker within a FAT gene that is associated with a bipolar affective disorder in a sample derived from the subject, wherein detection of said marker indicates that the subject is a carrier of a gene or allele of a gene or a polymorphism is associated with a bipolar affective disorder.
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- 25 37. A method of treatment or prophylaxis of a bipolar affective disorder comprising:
 - (i) performing the method of any one of claims 1 to 31 for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder; and
 - (ii) administering or recommending a therapeutic for the treatment of bipolar affective disorder.
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38. A method for identifying a marker that is associated with a bipolar affective disorder, said method comprising:
 - (i) identifying a polymorphism or allele within a FAT gene or an expression product thereof;
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- (ii) analyzing a panel of subjects to determine those that suffer from a bipolar affective disorder, wherein not all members of the panel comprise the polymorphism or allele; and
- 5 (iii) determining the variation in the development of a bipolar affective disorder wherein said variation indicates that the polymorphism or allele is associated with a subject's predisposition to a bipolar affective disorder.
39. A method for determining a candidate compound for the treatment of a bipolar affective disorder comprising:
- 10 (i) administering a candidate compound to an animal or cell comprising or expressing a marker within a FAT gene that is associated with a bipolar affective disorder and determining the level of FAT expression in said cell or animal;
- (ii) administering a candidate compound to an animal or cell that does not comprise or express a marker within a FAT gene that is associated with a bipolar affective disorder and determining the level of FAT expression in said cell or animal; and
- 15 (iii) comparing the level of FAT expression at (i) and (ii), wherein a decreased level of FAT expression at (i) relative to (ii) indicates that the compound is a candidate compound for the treatment of a bipolar affective disorder.
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40. A method for determining a candidate compound for the treatment of a bipolar affective disorder comprising:
- 25 (i) administering a candidate compound to an animal or cell capable of expressing a FAT gene and determining the level of FAT expression in said cell or animal;
- (ii) determining the level of FAT expression in an animal or cell capable of expressing a FAT gene in the absence of the candidate compound; and
- 30 (iii) comparing the level of FAT expression at (i) and (ii), wherein a decreased level of FAT expression at (i) relative to (ii) indicates that the compound is a candidate compound for the treatment of a bipolar affective disorder.
- 35 41. The method according to claim 39 or 40 wherein the level of FAT expression is determined by determining the level of FAT mRNA in the cell or animal.

42. A process for identifying or determining a compound or modulator for the treatment of a bipolar affective disorder said method comprising:

- 5 (i) performing the method according to any one of claims 39 to 41 to thereby identify or determine a compound for the treatment of a bipolar affective disorder;
- (ii) optionally, determining the structure of the compound;
- (iii) optionally, providing the name or structure of the compound; and
- (iv) providing the compound.

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43. A process of manufacturing a compound for the treatment of a bipolar affective disorder comprising:

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- (i) determining a candidate compound for the treatment of a bipolar affective disorder by performing the method according to any one of claims 39 to 41; and
- (ii) using the compound in the manufacture of a therapeutic or prophylactic for the treatment of bipolar affective disorder.